REMARKS

In view of the preceding amendments and the comments which follow, reconsideration of the Final Rejection of January 8, 2001 is respectfully requested by Applicants.

Claim 17 has been cancelled. Claims 23 and 24 have been amended to correct typographical errors. Claims 15, 20, 25, and 26 have been amended to limit the claimed pH range to between 8 and 10. Support for this pH range is found in the specification on page 3, line 18, on page 4, lines 2-3, and on page 4, lines 30-32.

Claims 15, 16, and 18-26 are currently pending in the application and stand finally rejected.

Rejections under 35 USC §103 (a)

Claims 15 and 17-20 have been rejected under 35 USC §103 (a) as being unpatentable over the Promega catalog, 1992-1993, page 170 (hereinafter "Promega") in view of the Perkin Elmer Cetus GeneAmp DNA Amplification Reagent Kit, 1988 (hereinafter "Perkin Elmer"). The Examiner argues that the Promega reference teaches an aqueous solution containing one or more nucleoside triphosphates wherein the pH value of said solution is 7.5 and wherein said solution is free of stabilizing substances. Although Promega doesn't teach a solution having a pH above 7.5, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the teaching of a pH of 7.5 encompasses minor variations in pH above the pH of 7.5, e.g., 7.5001. Alternatively, it would have been obvious to one skilled in the art to modify the 7.5 pH of Promega to a pH above 7.5, e.g., 7.5001, using routine experimentation to optimize solution conditions to thereby maximize experimental results.

As now amended, Claims 15 and 18-20 (Claim 17 having been cancelled) recite Applicants' preferred pH range of 8 to 10 as taught in their specification at page 3, line

18, at page 4, lines 2-3, and at page 4, lines 30-32. Applicants argue that such a pH range is not taught nor suggested by the prior art, nor is such a range obvious over the prior art nor even considered to be within experimental variation. A range of 8 to 10 cannot be said to encompass "minor variations in pH above 7.5, e.g., 7.5001". Further, a skilled artisan would not be led to use a pH range of 8 to 10 in routine experimentation in order to optimize solution conditions and thereby maximize experimental results because a range of 8 to 10 is sufficiently beyond the general conditions taught by the prior art and not merely a minor variation. That a solution comprising a nucleoside triphosphate is stabilized at a pH between 8 and 10 in the absence of stabilizing substances is an unexpected and surprising finding by the present inventors. The Examiner's reconsideration of the rejection of Claims 15 and 18-20 is respectfully requested.

Claims 16 and 26 have been rejected under 35 USC §103 (a) as being unpatentable over the Promega catalog, 1992-1993, page 170 (hereinafter "Promega") in view of the Gibco BRL catalog, 1993, page 300 (hereinafter "Gibco"). The Examiner argues that Promega teaches an aqueous solution containing one or more nucleoside triphosphates wherein the pH value of said solution is 7.5 and wherein said solution is free of stabilizing substances, but Promega does not teach that the nucleoside triphosphates are modified, e.g., dideoxynucleotides. However, modified nucleoside triphosphates, e.g., dideoxynucleotides, in aqueous solutions were well known in the art at the time the claimed invention was made as taught by Gibco. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the nucleoside triphosphates of Promega with the modified nucleoside triphosphates taught by Gibco for the expected benefit of providing detectable nucleosides based on the modification, e.g., termination of extension product. Additionally, it would have been obvious to one skilled in the art to modify the 7.5 pH of Promega to a pH above 7.5, e.g., 7.5001, using routine experimentation to optimize solution conditions to thereby maximize experimental results.

Claim 16 depends from Claim 15, and the patentability of Claim 15 over the prior art Promega reference has been argued above. The Gibco reference is relied upon for its teaching of modified nucleoside triphosphates and thus should not affect the patentability of a claim depending from a patentable parent claim.

Like Claim 15, Claim 26 as currently amended recites a solution comprising a nucleoside triphosphates at a pH range of 8 to 10 wherein the solution is free of stabilizing substances. Such a pH range is well beyond the general conditions and pH of 7.5 taught by the prior art, and increased stability of a solution comprising a nucleoside triphosphate at the pH range of 8 to 10 in the absence of stabilizing substances was an unexpected and surprising finding by the present inventors. The Examiner's reconsideration of the rejection of Claims 16 and 26 is respectfully requested.

Claims 21-25 have been rejected under 35 USC §103 (a) as being unpatentable over the Promega catalog, 1992-1993, page 170 (hereinafter "Promega") in view of the Perkin Elmer Cetus GeneAmp DNA Amplification Reagent Kit, 1988 (hereinafter "Perkin Elmer"). The claims are drawn to methods for replication of nucleic acid fragments (Claim 21), synthesizing nucleic acid sequences (Claim 22), random priming of nucleic acid sequences (Claim 23), nick translation of nucleic acid sequences (Claim 24) and synthesizing nucleic acid sequences via a polymerase chain reaction (Claim 25). The claimed methods are acknowledged by applicant as known in the art, the improvement being the methods comprising the solution according to Claim 15. Promega teaches the claimed solution and the use of the claimed solution as detailed below. Perkin Elmer was not relied upon for the rejection but was merely cited for the teaching of methods which applicant acknowledged as known in the art.

Regarding Claim 21, Promega teaches replicating nucleic acid fragments, i.e., cDNA synthesis comprising the solution of Claim 15 wherein the pH is 7.5.

Regarding Claim 22, Promega teaches synthesizing nucleic acid sequences, i.e., sequencing comprising the solution of Claim 15.

Regarding Claim 23, Promega teaches random priming, i.e., sequencing comprising the solution of Claim 15 wherein the pH is 7.5.

Regarding Claim 24, Promega teaches nick translation, i.e., labeling comprising the solution of Claim 15 wherein the pH is 7.5.

Regarding Claim 25, Promega teaches a solution containing one or more nucleoside triphosphates wherein the pH value of said solution is 7.5 and wherein said solution is free of stabilizing substances and wherein sequencing reactions comprise said solution.

Promega teaches the solution having a pH of 7.5 but does not teach the solution having a pH above 7.5. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the teaching of a pH of 7.5 encompasses minor variations in pH including a pH above the pH of 7.5, e.g., 7.5001. Alternatively, it would have been obvious to one skilled in the art to modify the 7.5 pH of Promega to a pH above 7.5, e.g., 7.5001, using routine experimentation to optimize experimental conditions to thereby maximize experimental results. The Examiner further cites *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 which states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation. Additionally, the skilled practitioner in the art would have been motivated to apply the solution of Promega to methods known in the art and to raise the assay solution pH from 7.5 to above 7.5 based on assay conditions taught by Perkin Elmer wherein the assay is performed in 25 mM TAPS-Cl, pH 9.3 for the benefit of economy of time and reagent cost by eliminating the need to adjust the pH of the assay solution to maintain the desired pH of 9.3 and to thereby optimize experimental conditions and maximize experimental results.

As now amended, all currently pending claims recite a pH range of 8 to 10. Claims 21-24 are dependent upon Claim 15, and the patentability of Claim 15 over the prior art Promega and Perkin Elmer references has been argued above. Claims 21-24 should enjoy the same patentability as Claim 15 from which they depend.

Like Claim 15, Claim 25 as currently amended recites solution comprising a nucleoside triphosphates at a pH range of 8 to 10 wherein the solution is free of stabilizing substances. Such a pH range is well beyond the general conditions and pH of 7.5 taught by the prior art, and increased stability of a solution comprising a nucleoside triphosphate at the pH range of 8 to 10 was an unexpected and surprising finding by the present inventors. Furthermore, the teaching of Perkin Elmer that the pH for storing the solution is less than the pH for performing the assay actually leads the skilled artisan to avoid storage of the solution at a higher pH, contrary to what the Examiner suggests. The Examiner's reconsideration of the rejection of Claims 21-25 is respectfully requested.

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Applicants submit that their application is now in condition for allowance, and favorable reconsideration of their application in light of the above remarks is respectfully requested. Allowance of claims 15, 16, and 18-26 at an early date is earnestly solicited.

The Examiner is hereby authorized to charge any fees associated with this amendment to Deposit Account No. 50-0877. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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CLAIMS LISTING 3/31/2004

What is claimed is:

1-14 (cancelled)

15. (currently amended) An aqueous solution comprising one or more nucleoside triphosphates, wherein the pH value of said solution is ~~above 7.5~~ between 8 and 10 and wherein said solution is free of stabilizing substances and a PCR function test is positive after about 90 days at a temperature of 35°C.

16. (previously presented) The solution of claim 15, wherein said nucleoside triphosphates are modified nucleoside triphosphates.

17. (cancelled)

18. (previously presented) The solution of claim 15, wherein the solution has a concentration of said nucleoside triphosphates of between about 2 to 200 mmol/l.

19. (previously presented) The solution of claim 15, wherein said nucleoside triphosphates are deoxynucleoside triphosphates.

20. (currently amended) The solution of claim 15, wherein said solution contains a substance which buffers at a ~~above~~ pH ~~7.5~~ between 8 and 10.

21. (previously presented) In a method for replicating nucleic acid fragments via a reaction in the presence of an enzyme with reverse transcriptase activity, said method comprising the addition of nucleoside triphosphates to said reaction, the improvement comprising the addition of a solution according to claim 15.

22. (previously presented) In a method for synthesizing nucleic acid sequences via a cycle sequencing reaction, said method comprising the addition of nucleoside triphosphates to said reaction, the improvement comprising the addition of a solution according to claim 15.

CLAIMS LISTING 3/31/2004

23. (currently amended) In a method for random priming of nucleic acid sequences in a reaction, said method comprising the addition of nucleoside triphosphates to ~~siad~~ said reaction, the improvement comprising the addition of a solution according to claim 15.

24. (currently amended) In a method for nick translation of nucleic acid sequences in a ~~reation~~ reaction, said method comprising the addition of nucleoside triphosphates to said reaction, the improvement comprising the addition of a solution according to claim 15.

25. (currently amended) In a method for synthesizing nucleic acid sequences via a polymerase chain reaction, said method comprising the addition of nucleoside triphosphates to said reaction, the improvement comprising the use of a solution containing one or more nucleoside triphosphates, wherein the pH value of said solution is ~~above 7.5~~ between 8 and 10 and wherein said solution is free of stabilizing substances and a PCR function test is positive after about 90 days at a temperature of 35°C.

26. (currently amended) An aqueous solution comprising one or more dideoxynucleotide triphosphates, wherein the pH value of said solution is ~~above 7.5~~ between 8 and 10 and wherein said solution is free of stabilizing substances and a PCR function test is positive after about 90 days at a temperature of 35°C.